

**AMENDMENTS TO THE CLAIMS:**

This listing of claims will replace all prior versions, and listings, of claims in the application:

1.-59. (Canceled).

60. (New) A process for the preparation of an N-acyl-(epi)K5-amine-O-oversulfate-derivative or of its chemically or pharmaceutically acceptable salts, which comprises

(a) treating an (epi)K5-N-sulfate-derivative, in acidic form, with a tertiary or quaternary organic base, letting the reaction mixture to stand for a time period of 30-60 minutes, maintaining the pH of the solution at a value of approximately 7 and isolating its salt with said organic base;

(b) treating said organic base salt of said (epi)K5-N-sulfate-derivative with an O-sulfation reagent in the conditions of O-oversulfation; and

(c) treating the (epi)K5-amine-O-oversulfate-derivative thus obtained with a functional derivative of a C<sub>2</sub>-C<sub>4</sub> carboxylic acid and isolating the N-acyl-(epi)K5-amine-O-oversulfate-derivative.

61. (New) Process according to claim 60, wherein said N-acyl-(epi)K5-amine-O-oversulfate is isolated in sodium salt form and optionally transformed into another chemically or pharmaceutically acceptable salt.

62. (New) Process according claim 60, wherein, in step (a), tetrabutylammonium hydroxide is used as an organic base.

63. (New) Process according to claim 60, wherein in step (b) the O-oversulfation is carried out in dimethylformamide utilizing 2-4 moles of O-sulfation reagent per available OH per disaccharide at a temperature of 40-60°C for 15-20 hours.

64. (New) Process according to claim 60, wherein as starting material an (epi)K5-N-sulfate-derivative is used having a mean molecular weight from approximately 1,000 to approximately 25,000.

65. (New) Process according to claim 60, wherein said starting material is 40-60% C5-epimerized.

66. (New) Process according claim 60, wherein said starting material has a mean

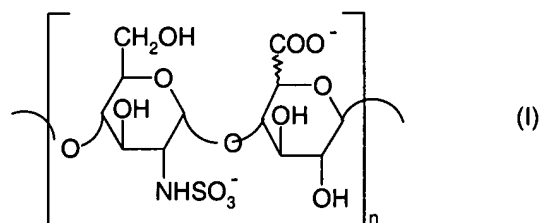
molecular weight from approximately 1,500 to approximately 25,000.

67. (New) Process according to claim 66, wherein said starting material has a mean molecular weight between 10,000 and 25,000.

68. (New) Process according to claim 66, wherein said starting material has a mean molecular weight from approximately 1,500 to approximately 12,000.

69. (New) Process according to claim 68, wherein said starting material has a mean molecular weight from approximately 1,500 to approximately 8,000.

70. (New) Process according to claim 60, wherein as starting material an (epi)K5-N-sulfate-derivative is used consisting of a chain mixture in which at least 90% of said chains have the formula I

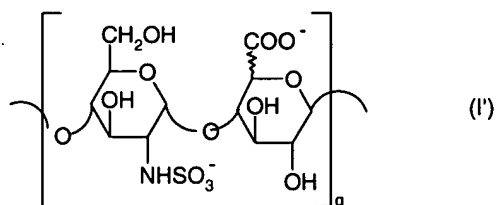


in which the glucuronic units/iduronic units ratio is from 100/0 to 40/60, n is an integer from 2 to 100 and the corresponding cation is chemically or pharmaceutically acceptable.

71. (New) Process according to claim 70, wherein said starting material consists of a chain mixture in which at least 90% of said chains have the formula I, in which the uronic units are 40-60% consisting of iduronic acid.

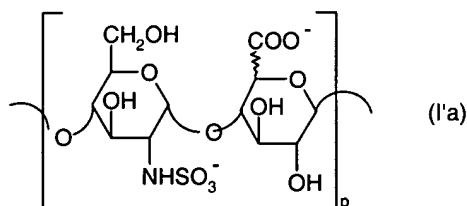
72. (New) Process according to claim 70, wherein said starting material is a LMW-(epi)K5-N-sulfate consisting of a chain mixture in which at least 90% of said chains have the formula I in which the uronic units are all consisting of glucuronic acid or are 40-60% consisting of iduronic acid, n is an integer from 3 to 15 and the corresponding cation is chemically acceptable.

73. (New) Process according to claim 70, wherein said starting material is a MW-(epi)K5-N-sulfate consisting of a chain mixture in which at least 90% of said chains have the formula I'



in which the uronic units are 100% consisting of glucuronic acid or 60-40% of glucuronic acid and 40-60% of iduronic acid, q is an integer from 2 to 20 and the corresponding cation is chemically or pharmaceutically acceptable.

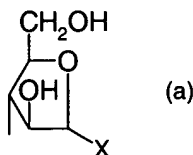
74. (New) Process according to claim 70, wherein said starting material is a LMW-(epi)K5-N-sulfate consisting of a chain mixture in which the preponderant species has the formula I'a



in which the uronic units are 100% consisting of glucuronic acid or 60-40% glucuronic and 40% to 60% of iduronic acid, p is an integer from 4 to 8.

75. (New) Process according to claim 64, wherein said starting material is a LMW-(epi)K5-N-sulfate obtained by nitrous depolymerization of the corresponding (epi)K5-N-sulfate and subsequent reduction.

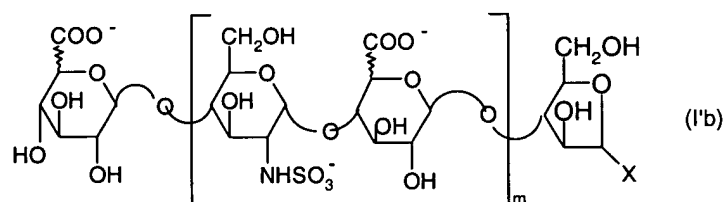
76. (New) Process according to claim 75, wherein said starting LMW-(epi)K5-N-sulfate contains, at the reducing end of the majority of the chains in said chain mixture, a 2,5-anhydromanno unit of structure (a)



in which X represents a hydroxymethyl group.

77. (New) Process according to claim 75, wherein as starting material a LMW-(epi)K5-N-sulfate is used consisting of chain mixtures in which the preponderant species is a compound

of formula I'b



in which X is hydroxymethyl, m is 4, 5 or 6, the corresponding cation is a chemically or pharmaceutically acceptable ion, the uronic units are all of glucuronic acid or the glucuronic and iduronic units are present alternately, starting with a glucuronic or iduronic unit.

78. (New) Process according to claim 60, wherein said starting (epi)K5-N-sulfate-derivative is utilized in sodium salt form.

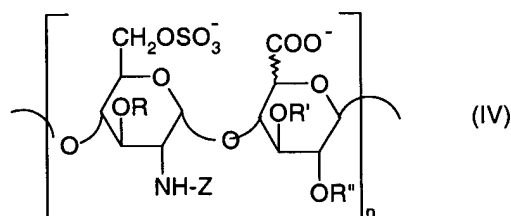
79. (New) A 100% acylated N-acyl-epiK5-amine-O-oversulfate-derivative, in which acyl is a (C<sub>2</sub>-C<sub>4</sub>)acyl, having an iduronic acid content of 20-60%, a mean molecular weight from approximately 2,000 to approximately 45,000 and a sulfation degree of at least 3.4, or one of its chemically or pharmaceutically acceptable salts.

80. (New) An N-acyl-epiK5-amine-O-oversulfate-derivative according to claim 79, whose mean molecular weight is between approximately 15,000 and approximately 45,000.

81. (New) An N-acyl-epiK5-amine-O-oversulfate-derivative according to claim 79, whose mean molecular weight is between approximately 4,500 and approximately 8,500.

82. (New) An N-acyl-epiK5-amine-O-oversulfate-derivative according to claim 79, wherein said degree of sulfation is from 3.4 to 3.8.

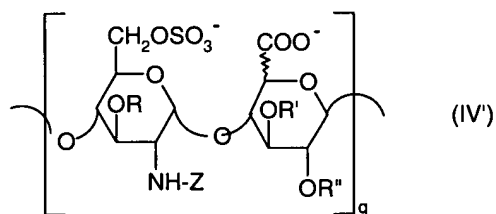
83. (New) A 100% N-acylated N-acyl-epiK5-amine-O-oversulfate-derivative consisting of chain mixtures in which at least 90% of said chains have the formula IV



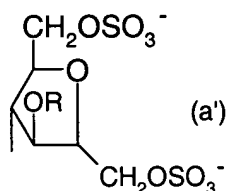
in which the uronic units are 20-60% consisting of iduronic acid, n is an integer from 2 to 100, R, R' and R'' are hydrogen or SO<sub>3</sub><sup>-</sup>, Z is (C<sub>2</sub>-C<sub>4</sub>)acyl, the degree of sulfation is at least 3.4 and the corresponding cation is chemically or pharmaceutically acceptable.

84. (New) A N-acyl-epiK5-amine-O-oversulfate-derivative according to claim 83, consisting of a chain mixture in which at least 90% of said chains have the formula IV in which the uronic units are 40-60% consisting of iduronic acid, n is a integer from 3 to 100, with a mean molecular weight from approximately 2,000 to approximately 45,000, R is at least 40%  $\text{SO}_3^-$ , R' and R'' are both  $\text{SO}_3^-$  or one is hydrogen and the other is 5-10%  $\text{SO}_3^-$  in monosulfate glucuronic acid and 10-15%  $\text{SO}_3^-$  in monosulfate iduronic acid and the corresponding cation is chemically or pharmaceutically acceptable.

85. (New) A N-acyl-epiK5-amine-O-oversulfate-derivative according to claim 83, which is a LMW-N-acyl-epiK5-O-oversulfate consisting of a chain mixture in which at least 90% of said chains have the formula IV'

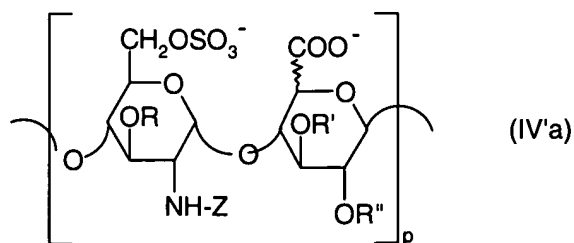


in which q is an integer from 2 to 20, R, R' and R'' represent hydrogen or an  $\text{SO}_3^-$  group for a degree of sulfation from 3.55 to 4, Z is  $(\text{C}_2\text{-C}_4)$ acyl, bearing a sulphated 2,5-anhydromannitol unit of structure (a')



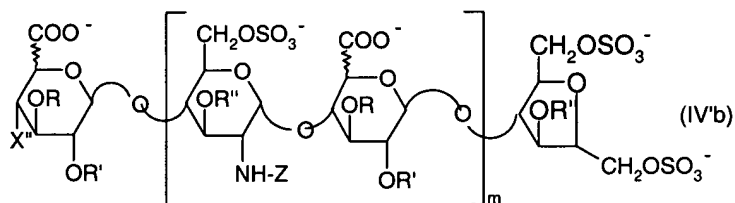
wherein R represent hydrogen or  $\text{SO}_3^-$ , in the majority of the chains in said chain mixture, and the corresponding cation is chemically or pharmaceutically acceptable.

86. (New) A LMW-N-acyl-epiK5-amine-O-oversulfate according to claim 85, consisting of a chain mixture in which the preponderant species is a compound of formula IV'a



in which  $p$  is an integer from 4 to 8,  $R$ ,  $R'$  and  $R''$  are hydrogen or an  $\text{SO}_3^-$  group for a degree of sulfation from 3.55 to 4,  $Z$  is  $(\text{C}_2\text{-C}_4)$ acyl, and the corresponding cation is chemically or pharmaceutically acceptable.

87. (New) A LMW-N-acyl-epiK5-amine-O-oversulfate according to claim 86, wherein said preponderant species is a compound of formula IV'b

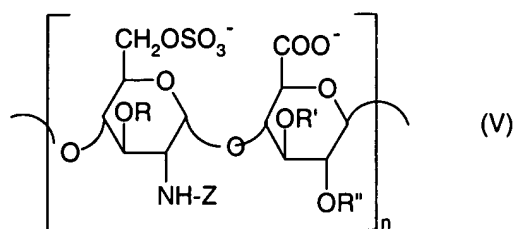


in which  $R$ ,  $R'$  and  $R''$  are hydrogen or  $\text{SO}_3^-$ ,  $Z$  is  $(\text{C}_2\text{-C}_4)$ acyl,  $X''$  is  $\text{OH}$  or  $\text{OSO}_3^-$ ,  $m$  is 4, 5 or 6, for a degree of sulfation from 3.55 to 4, the uronic units are present alternately, starting with a glucuronic or iduronic unit, and the corresponding cation is chemically or pharmaceutically acceptable.

88. (New) A N-acyl-epiK5-amine-O-oversulfate-derivative according to claim 79 in which the substituent  $(\text{C}_2\text{-C}_4)$ acyl is selected from the group consisting of acetyl, (2-carboxy)acetyl, (2-methoxycarbonyl)acetyl, (2-ethoxycarbonyl)acetyl, propionyl, (3-carboxy)propionyl, N-(3-methoxycarbonyl)propionyl and (3-ethoxycarbonyl)propionyl.

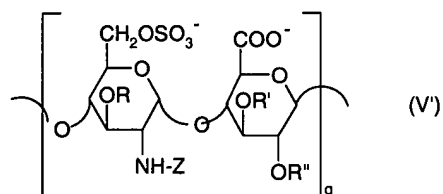
89. (New) An N-acyl-epiK5-amine-O-oversulfate-derivative according to claim 79, wherein said salt is an alkaline metal or alkaline-earth metal, ammonium,  $(\text{C}_1\text{-C}_4)$ tetraalkylammonium, aluminum or zinc salt.

90. (New) A 100% acylated N-acyl-K5-amine-O-oversulfate-derivative consisting of a chain mixture in which at least 90% of said chains have the formula V

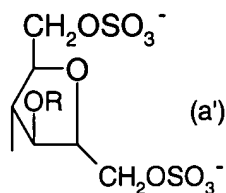


in which  $n$  is an integer from 2 to 100,  $Z$  is  $(C_2-C_4)$ acyl,  $R$ ,  $R'$  and  $R''$  are hydrogen or  $SO_3^-$ , the degree of sulfation is from 2.2 to 3, and the corresponding cation is chemically or pharmaceutically acceptable.

91. (New) A N-acyl-K5-amine-O-oversulfate-derivative according to claim 90, which is a LMW-N-acyl-K5-amine-O-oversulfate consisting of a chain mixture in which at least 90% of said chains have the formula V'

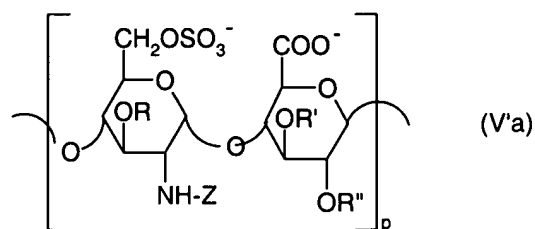


in which  $q$  is an integer from 2 to 20,  $Z$  is  $(C_2-C_4)$ acyl,  $R$ ,  $R'$  and  $R''$  represent hydrogen or an  $SO_3^-$  group for a degree of sulfation from 2.2 to 3, the majority of the chains in said chain mixture bearing a sulphated 2,5-anhydromannitol unit of structure (a')



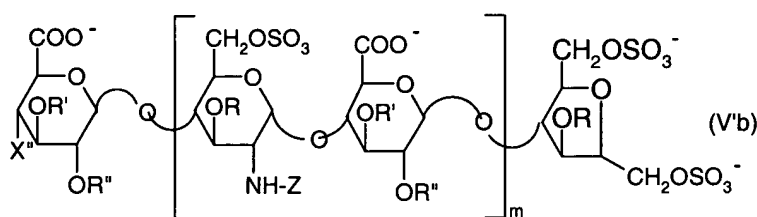
wherein  $R$  represent hydrogen or  $SO_3^-$ , and the corresponding cation is chemically or pharmaceutically acceptable.

92. (New) A LMW-N-acyl-K5-amine-O-oversulfate according to claim 91, consisting of a chain mixture in which the preponderant species is a compound of formula V'a



in which  $p$  is an integer from 4 to 8,  $Z$  is  $(C_2-C_4)$ acyl,  $R$ ,  $R'$  and  $R''$  represent hydrogen or an  $SO_3^-$  group for a degree of sulfation from 2.2 to 3, and the corresponding cation is chemically or pharmaceutically acceptable.

93. (New) A LMW-N-acyl-K5-amine-O-oversulfate according to claim 92, wherein said preponderant species is a compound of formula V'b



in which  $Z$  is  $(C_2-C_4)$ acyl,  $R$ ,  $R'$  and  $R''$  are hydrogen or  $SO_3^-$ ,  $X''$  is  $OH$  or  $OSO_3^-$ , for a degree of sulfation from 2.2 to 3,  $m$  is 4, 5 or 6 and the corresponding cation is a chemically or pharmaceutically acceptable ion.

94. (New) A N-acyl-K5-amine-O-oversulfate-derivative according to claim 90 wherein said degree of sulfation is from 2.3 to 3.

95. (New) A N-acyl-K5-amine-O-oversulfate-derivative according to claim 94, wherein said degree of sulfation is from 2.5 to 3.

96. (New) A N-acyl-K5-amine-O-oversulfate-derivative according to claim 95, wherein said degree of sulfation is from 2.7 to 2.9.

97. (New) A N-acyl-K5-amine-O-oversulfate-derivative according to claim 90, wherein the substituent  $(C_2-C_4)$ acyl is different from acetyl.

98. (New) A N-acyl-K5-amine-O-oversulfate-derivative according to claim 90, in which the substituent  $(C_2-C_4)$ acyl is acetyl, having a degree of sulfation of 2.7-2.9.

99. (New) An N-acyl-K5-amine-O-oversulfate-derivative according to claim 98, having



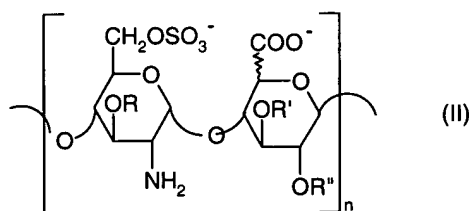
a degree of sulfation of approximately 2.8.

100. (New) A N-acyl-K5-amine-O-oversulfate-derivative according to claim 90, wherein said salt is an alkaline metal, alkaline-earth metal, ammonium, (C<sub>1</sub>-C<sub>4</sub>)tetraalkylammonium, aluminum or zinc salt.

101. (New) A pharmaceutical composition including, as an active ingredient, an (epi)K5-amine-O-oversulfate-derivative or one of its pharmaceutically acceptable salts, isolated in sodium salt form and optionally transformed into another pharmaceutically acceptable salt, in mixture with a pharmaceutical excipient.

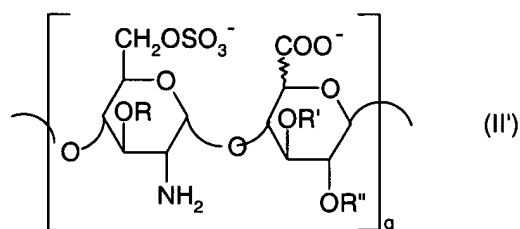
102. (New) Composition according to claim 101, wherein said active ingredient is an (epi)K5-amine-O-oversulfate-derivative having a mean molecular weight from approximately 4,500 to approximately 40,000.

103. (New) Pharmaceutical composition according to claim 101, in which said active ingredient is an (epi)K5-amine-O-oversulfate-derivative consisting of a chain mixture in which at least 90% of said chains have the formula II

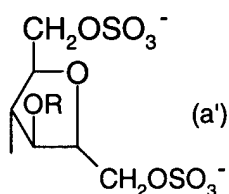


in which n is an integer from 2 to 100, R, R' and R'' are hydrogen or SO<sub>3</sub><sup>-</sup>, the uronic units are all of glucuronic acid, for a degree of sulfation from 2.2 to 3, or are 20-60% consisting of iduronic acid, for a sulfation degree of at least 3.4, and the corresponding cation is pharmaceutically acceptable.

104. (New) Pharmaceutical composition according to claim 103, wherein said active ingredient is a LMW-epiK5-amine-O-oversulfate consisting of a chain mixture in which at least 90% of said chains have the formula II'



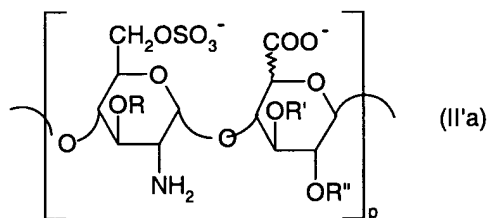
in which  $q$  is an integer from 2 to 20,  $R$ ,  $R'$  and  $R''$  are hydrogen or  $\text{SO}_3^-$ , the uronic units are 20-60% those of iduronic acid, for a degree of sulfation from 3.55 to 4, and bearing a sulphated 2,5-anhydromannitol unit of structure (a')



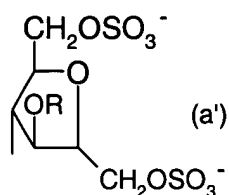
wherein  $R$  represent hydrogen or  $\text{SO}_3^-$ , in the majority of the chains in said chain mixture.

105. (New) Pharmaceutical composition according to claim 104, wherein, in said chain mixture of formula II', the uronic units are 40-60% consisting of iduronic acid,  $R$  is at least 40%  $\text{SO}_3^-$ ,  $R'$  and  $R''$  are both  $\text{SO}_3^-$  or one is hydrogen and the other is 5-10%  $\text{SO}_3^-$  in glucuronic acid and 10-15%  $\text{SO}_3^-$  in iduronic acid,  $n$  is an integer from 3 to 15, with a mean molecular weight from approximately 4,000 to approximately 8,000.

106. (New) Pharmaceutical composition according to claim 104, wherein said LMW-epiK5-amine-O-oversulfate is consisting of a chain mixture in which the preponderant species has the formula II'a

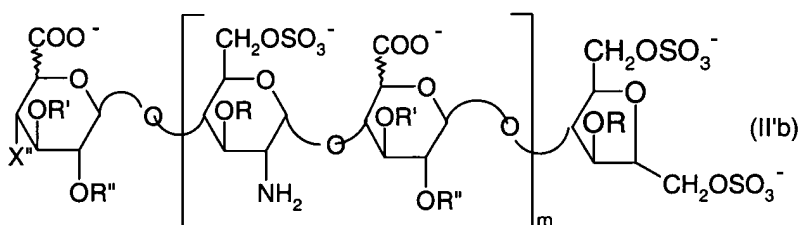


in which  $p$  is an integer from 4 to 8,  $R$ ,  $R'$  and  $R''$  are as defined above, the degree of sulfation is from 3.55 to 4, said preponderant species bearing a sulphated 2,5-anhydromannitol unit of structure (a')



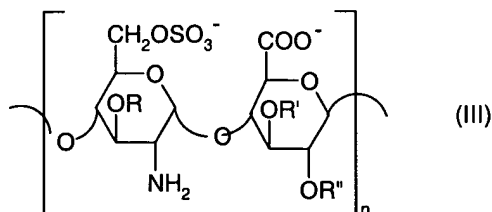
wherein R represent hydrogen or  $\text{SO}_3^-$ , in the majority of its chains in said chain mixture and the corresponding cation is pharmaceutically acceptable.

107. (New) Pharmaceutical composition according to claim 106, wherein said preponderant species is a compound of formula II'b



in which R, R' and R'' are hydrogen or  $\text{SO}_3^-$ , X'' is OH or  $\text{OSO}_3^-$ , m is 4, 5 or 6, the uronic units are 40-60% consisting of iduronic acid, for a degree of sulfation from 3.55 to 4, the iduronic units being present alternately, starting with a glucuronic or iduronic unit, and the corresponding cation is a pharmaceutically acceptable ion.

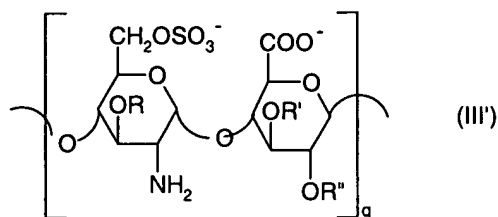
108. (New) Pharmaceutical composition according to claim 101 including, as an active ingredient, a K5-amine-O-oversulfate-derivative consisting of a chain mixture in which at least 90% of said chains have the formula III



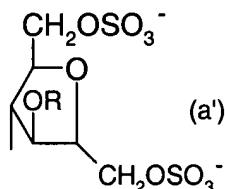
in which n is a integer from 2 to 100, R, R' and R'' are hydrogen or  $\text{SO}_3^-$ , the degree of sulfation is at least 2.2, and the corresponding cation is pharmaceutically acceptable.

109. (New) Pharmaceutical composition according to claim 108, wherein said active

ingredient is a LMW- K5-amine-O-oversulfate consisting of a chain mixture in which at least 90% of said chains have the formula III'

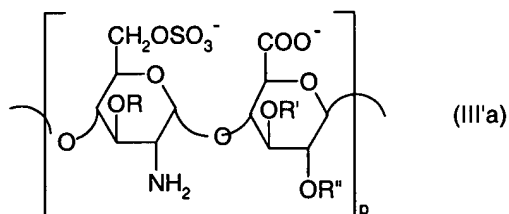


in which q is an integer from 2 to 20, R, R' and R'' represent hydrogen or a SO<sub>3</sub><sup>-</sup> group for a sulfation degree of at least 2.2, and at the reducing end of the majority of the chains in said chain mixture presents a sulphated 2,5-anhydromannitol unit of structure (a')



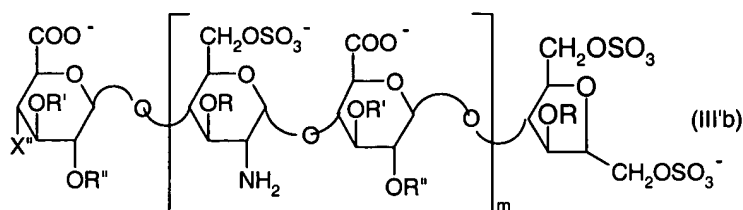
wherein R represents hydrogen or SO<sub>3</sub><sup>-</sup>.

110. (New) Pharmaceutical composition according to claim 109, wherein said LMW- K5-amine-O-oversulfate consists of a chain mixture in which the preponderant species has the formula III'a



in which p is an integer from 4 to 8, R, R' and R'' are as defined above, the degree of sulfation being from 2.2 to 3.

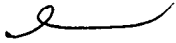
111. (New) Pharmaceutical composition according to claim 106, wherein said preponderant species is a compound of formula III'b



in which R, R' and R'' are hydrogen or  $\text{SO}_3^-$ , X'' is OH or  $\text{OSO}_3^-$ , for a degree of sulfation from 2.2 to 3, m is 4, 5 or 6 and the corresponding cation is a pharmaceutically acceptable ion.

112. (New) Pharmaceutical composition according to claim 101, wherein said pharmaceutically acceptable salt or cation is sodium, potassium, calcium, magnesium or zinc.

113. (New) Pharmaceutical composition according to claim 101, which is in the form of cream, ointment, liniment, gel, foam, balsam, vaginal pessary, suppository, solution or suspension for local administration.

114. (New) A pharmaceutical composition containing, as an active ingredient, a  pharmacologically active amount of a LMW-(epi)K5-N-sulfate basically free of acetyl groups, or of one of its pharmaceutically acceptable salts, in mixture with a pharmaceutical excipient.

115. (New) A cosmetic composition containing an effective amount of a LMW-(epi)K5-N-sulfate basically free of acetyl groups, or of one of its pharmaceutically acceptable salts, in mixture with a cosmetic excipient.